Malignant Mesothelioma Cancer

Malignant mesothelioma is a rare, aggressive cancer arising from **mesothelial cells** lining the **pleura, peritoneum, pericardium** , or **tunica vaginalis** of the testis. It results from uncontrolled proliferation and invasion of these cells.

Anatomy of Mesothelium

- **Mesothelium** : A membrane lining body cavities and organs.
- **Visceral mesothelium** : Covers internal organs.
- **Parietal mesothelium** : Lines the body walls.

Epidemiology

- ~3,000 new cases/year in the USA.
- 80% are **pleural mesotheliomas** (most common form).
- Latency: 20–50 years post asbestos exposure.
- Median diagnosis age: ~60 years.
- Male predominance: 5:1 male to female ratio.
- Risk varies with occupation (shorter latency in dock workers and insulators; longer in maritime and ship workers).
- Lifetime risk ~0.5–1%.

Etiology and Risk Factors

- **Primary cause** : Asbestos exposure.
    - Blue asbestos (crocidolite) > Brown asbestos (amosite) > White asbestos (chrysotile) in carcinogenic potential.
- ~50% of patients have no known asbestos exposure.
- Simian Virus 40 (SV40) DNA found in 60–83% of tumors, suggesting a cofactor role.
    - SV40 inactivates tumor suppressors **p53** and **Rb** .
- Reactive oxygen species from asbestos cause DNA damage.
- Familial and secondary household exposure possible.
- Children rarely show asbestos exposure.
- No specific chromosomal abnormalities are consistently associated.

Pathogenesis

- Asbestos fibers induce chronic inflammation and genetic damage.
- Carcinogenicity depends on fiber type and shape (needle-shaped fibers more carcinogenic).
- Disease progression involves local invasion and lymphatic spread.

Clinical Features

- Majority present with **pleural effusion** or **ascites** .
- Symptoms (90% intrathoracic):
  - Persistent cough
  - Chest wall pain (non-pleuritic)
  - Dyspnea
  - Unilateral chest wall dullness and decreased expansion
- Systemic symptoms:
  - Fever of unknown origin
  - Night sweats
  - Weight loss, anorexia
- Rare:
  - Cardiac arrhythmias, dysphagia (mediastinal involvement)
  - Thrombocytosis, DIC, thrombophlebitis, hemolytic anemia

Physical Exam & Imaging

- **Chest X-ray** :
  - Pleural-based nodular, irregular masses
  - Pleural thickening (>1 cm)
  - Pleural plaques (due to asbestos)
  - Moderate-large pleural effusion, usually unilateral (right side more common)
- **CT Scan** :
  - Defines extent of pleural/peritoneal tumor
  - Detects pleural thickening, fissure involvement, calcifications
  - Differentiates benign vs malignant pleural thickening but not primary vs metastatic
- **MRI and PET** : Used for staging and extent assessment.
- Pulmonary function tests: Restrictive pattern common.

Spread

- Local invasion to lung, chest wall, mediastinum, diaphragm.
- Thoracic lymph node involvement in ~70%.
- Hematogenous metastases: liver, lung, kidney, adrenal, bone (rare).

Diagnosis

- Cytology of pleural fluid has low sensitivity.
- Biopsy required for definitive diagnosis:
  - **Thoracoscopic biopsy** preferred.
  - Percutaneous needle biopsy diagnostic in ~60% cases.
  - Open biopsy sometimes needed.
  - Tumor seeding possible along biopsy tract; prophylactic radiotherapy may prevent nodule growth.
- Pathology can mimic lung adenocarcinoma.
- Serum markers (experimental):
  - Osteopontin
  - Soluble mesothelin-related proteins (SMRP)

Staging (Pleural Mesothelioma)

- **Stage I** : Tumor limited to pleura; may involve ipsilateral lung, pericardium, or diaphragm; no lymph nodes.
- **Stage II** : Tumor plus ipsilateral lymph node involvement.
- **Stage III** : Tumor invades chest wall, heart, esophagus, or other thoracic structures; ipsilateral lymph nodes may be involved.
- **Stage IV** : Advanced tumor involving contralateral pleura or distant metastases.

(No established staging for peritoneal mesothelioma)